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EDITORIAL

SARS-CoV-2 AND ONCOLOGY

L. Fratino [1], D. Serraino [2]

[1] Oncologia Medica dei Tumori Immunocorrelati, Centro di Riferimento Oncologico (CRO), IRCCS, Aviano, Italy
[2] SOC Epidemiologia Oncologica, Centro di Riferimento Oncologico (CRO), IRCCS, Aviano, Italy

CORRESPONDING AUTHOR:

Diego Serraino
SOC Epidemiologia Oncologica
Centro di Riferimento Oncologico (CRO), IRCCS
via Franco Gallini 2
33081 Aviano, Italy
E-mail: serrainod@cro.it
ORCID: 0000-0003-0565-8920

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SARS-CoV-2; COVID-19; Oncology; research; impact.

IMPACT STATEMENT

This paper discusses open questions posed by the disruption of health systems -with focus on cancer- caused by the SARS-CoV-2 pandemic.

The impact of infection with the severe acute respiratory syndrome 2 (SARS-CoV-2) coronavirus, and the subsequent illness COVID-19, on people who suffer from neoplastic diseases remains one of the crucial health issues in the COVID-19 era. Its importance has been well recognized and evaluated since the early phase of the pandemic (1). As of March 2021, more than 10,000 articles have been published in the medical literature with regard to the impact of SARS-CoV-2 infection in people with cancer (2). It is worth stressing that, worldwide, more than 15 million people are diagnosed with cancer every year, while about 50 million people are already living after a cancer diagnosis (3). How will COVID-19 modify the life of these individuals already living with cancer, and the life of the millions that will be diagnosed in the coming years?

The interruption caused by SARS-CoV-2 infection on health systems has led hospitals to suspend non urgent cancer diagnostic procedures and treatments, while cancer patients have been discouraged from seeking care at scheduled intervals. After one year in the pandemic and the starting of vaccine availability, the question of how long will the SARS-CoV-2 pandemic last and what effect will it have on primary (*e.g.*, smoking, overweight, physical activity) and secondary prevention (*i.e.*, screening), diagnosis, treatment and care of cancer patients is still looking for numerous answers. Available evidence is largely heterogenous, depending on two groups of factors. Biologic (*e.g.*, immune depression related to anti-cancer treatments) and non-biologic factors (*e.g.*, most people with cancer needs to interface with health institu-

tions) have been hypothesized to expose cancer patients at higher risk of SARS-CoV-2 infection and, as a consequence, at higher risk of morbidity and mortality than correspondent uninfected cancer patients (4-6). As a consequence of persisting uncertainties, it is still difficult to predict how any change of practice will negatively affect cancer prognosis and outcomes (*e.g.*, overall survival). Similarly, it is still largely unpredictable how much the potential discrimination of SARS-CoV-2 infected cancer patients in context like drugs delivery, admission in intensive care units, screening tests (*e.g.*, mammogram for breast cancer, fecal occult blood test for colon cancer, HPV test for cervical cancer) will negatively impact on the number and the stage at presentation of new cancer cases.

In the pre-COVID 19 era, cancer guidelines shaped by national and international scientific societies have greatly contributed to efficiently fight cancer. Oncologists and other professionals of the Oncology fields are well aware of how guidelines were based on robust evidence accumulated worldwide in the last decades. It should be recognized that, in the meantime, recommendations and guidelines for the management of cancer patients in the context of SARS-CoV-2 infection are widely produced outside the traditional "Evidence Based" benchmark.

Thus, this is primarily the time for clear cut questions, including the following ones: what is the relationship between SARS-CoV-2 infection, cancer and immune suppression? Is there evidence that cancer patients undergoing chemotherapy, radiotherapy or surgery are more likely to acquire SARS-CoV-2 infection than patients treated for, as an example, myocardial infarction? Is the prognosis of cancer patients eventually infected with SARS-CoV-2 worse than that of age and gender analogous non infected patients? What is the effect of diagnostic delay on early diagnosis (*e.g.* how much will it negatively affect the neoplastic course of cancer) or the inclusion of cancer patients into randomized clinical trials?

Although those are open questions, several review articles have already summarized available data on the spread and clinical outcomes of SARS COV 2 infection in cancer patients. The prevalence of SARS-CoV-2 among cancer patients greatly varied according to study design, place and time of investigations. In Italy, out of 4789 cancer patients tested in the first months of the pandemic in the Veneto region, 723 (15.1%) turned out to have acquired SARS-CoV-2 infection (4). Conversely, SARS-CoV-2 infection was documented among only 0.7% of 59989 Italian cancer patients undergoing active antitumor treatment according to the findings of a retrospective nation-wide study (5). Lack of excess of SARS-CoV-2 infection has been documented in a clinical cohort of 1.016 patients with cancer history in Austria. Only four of them (0.4%) turned out to be have acquired SARS-CoV-2 infection, a proportion comparable to that measured among non-cancer patients (7).

Other investigations have indirectly assessed the prevalence of SARS-CoV-2 infection by estimating the proportion of cancer patients among examined people. For instance, 6%-7% of COVID-19 patients hospitalized in New York turned out to be cancer patients, a proportion higher than expected according to cancer prevalence in the corresponding general population (8, 9).

Adverse outcomes and increased risk of death have been already documented in cancer patients with SARS-CoV-2 infection (10-12). A pooled analysis of 52 studies published as of July 2020 estimated a high probability of death for infected cancer patients, with a case fatality rate of 25.6% (13). Findings from an international cohort study identified factors associated with an increased risk of 30-day mortality, including ageing, male sex, smoking and the presence of comorbidities (14). Among 1.004 cancer patients enrolled in the UK Coronavirus Cancer Monitoring Project, the all-cause risk of death in cancer patients with SARS-CoV-2 infection was associated with increasing age, and was particularly elevated in patients with hematological malignancies, a 2.25 fold increase for patients with leukemia, and a 2.09 fold increase for those hematological patients treated with chemotherapy (10). It has also been estimated that the COVID-19 diagnostic delay in the United Kingdom could cause in the next 5 years up to a 9.6% increased in death rate for breast cancer, 16.6% for colon-rectal cancer, 5.3% for lung cancer and 6.0% for esophageal cancer (12). In northern Italy, adverse outcomes, including death, were significantly more elevated in persons with SARS-CoV-2 infection and cancer than in persons with SARS-CoV-2 infection without cancer (4, 15).

Based on ongoing evidence, guide lines have been promptly circulated by scientific associations, including the European Society of Medical Oncology (ESMO) (16). Similar documents were issued in Italy for the management of cancer patients in the COVID-19 era by the medical community (17-19).

The COVID-19 pandemic has thus urged the cancer community to envisage a hardly hypothesized scenario – the presence of a new actor in the cancer drama- that pose unexpected challenges to public health, cancer patients, clinicians and researchers. The numerous studies already published on the relationships between COVID-19 and cancer have undoubtedly helped to focus major questions and immediate solutions. To further limit the disruption to cancer care caused by the COVID-19 pandemic, the persistence of scientific research at the pace of the one carried out in the first year of the pandemic will be of utmost importance.

ETHICS

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Conflict of interests

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Authors' contribution

All the authors contributed equally to conception, data collection, analysis and writing of this paper.

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RESEARCH ARTICLE

PROGNOSTIC ROLE OF THE PRIMARY TREATMENT IN THE NATURAL HISTORY OF OVARIAN CANCER: A PILOT STUDY

A. M. Perrone [1], M. Tesei [1], E. De Crescenzo [1], C. A. Coadă [2], A. Bovicelli [1,3], S. Boussedra [1], G. Dondi [1], S. Giunchi [1], P. De Iaco [1,3]

[1] Division of Oncologic Gynaecology, IRCCS, Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy
[2] Center for Applied Biomedical Research, Alma Mater Studiorum, University of Bologna, Bologna, Italy
[3] University of Bologna, Bologna, Italy

CORRESPONDING AUTHOR:

Anna Myriam Perrone
IRCCS Azienda Ospedaliero-Universitaria di Bologna
Division of Oncologic Gynaecology
via Giuseppe Massarenti 9
40138 Bologna, Italy
E-mail: myriam.perrone@aosp.bo.it
ORCID: 0000-0003-3140-4772

Doi: 10.48286/aro.2021.13

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ABSTRACT

Epithelial Ovarian cancer is the most lethal and silent gynaecological tumor and relapses in about 75% of cases. Retrospective data supported the superiority of secondary cytoreduction surgery (SCS) plus chemotherapy versus chemotherapy alone; in order to best select patients for SCS literature established a clinical score based on ascites, performance status, and absence of residual disease to primary surgery. The present study analyzed the outcomes and pattern of relapse of a population with first relapse of ovarian cancer undergoing secondary surgery without residual tumor divided into two groups based on the type of treatment at the first diagnosis (primary debulking surgery [PDS] or neoadjuvant chemotherapy followed by interval debulking surgery [IDS]).

This is an observational retrospective study carried out at the referred Centre of Oncologic Gynaecology of Bologna, Italy on patients who underwent SCS for ovarian cancer between January 2009 and December 2019 retrieved in an electronic database. Clinical surgical and pathological data were analyzed. Data about time and pattern of relapse and overall survival were evaluated.

Out of 270 ovarian cancer patients, 69 were enrolled in the study; 49 patients who at first received primary surgery (Group 1) and 20 patients at first received interval surgery (Group 2). The 5-year